

### **REMARKS/ARGUMENTS**

With this Amendment, claims 2, 3, 7, 9, 10, 14-20, 25, 26, 33-39, 41-45, 61, 62, and 82-91 are pending. Claims 1, 4-6, 8, 11-13, 21-24, 27-32, 40, 46-60 and 63-81 have been cancelled. Claims 84-91 are new. Applicants respectfully request entry of this Amendment because the pending claims are in condition for allowance.

#### **Claims Amendments**

Previously pending claims 1-81 have either been cancelled or amended to depend from one of independent claims 82 or 90. Previously pending claim 82 has been amended to recite that the tissue marker consists of a single zirconium oxide substrate and a coating, wherein the marker has an elongate shape and a length of between about 800 and about 3500 microns. New claim 89 is similar to claim 82, but recites a zirconium oxide body. Support for the shape and size limitations of these claims can be found, for example, on page 13 of the application as originally filed. For example, the specification teaches that the marker may have a length between about 800 and 3500 microns. The specification further teaches a variety of elongate shapes including, for example, dog bone, bar bell, rod and tube shapes.

New claims 90 and 91 recite a method of identifying an anatomical site for treatment including the steps of implanting only a tissue marker consisting of a single zirconium oxide substrate and a coating (claim 90) disposed thereon, forming a first X-ray image in which the marker is detectable and distinguishable from the anatomical site and forming a second magnetic field image of the anatomical site in which the marker is detectable without substantial image distortion. This method is clearly described throughout the specification.

#### **Replacement Drawings**

The Examiner objected to the drawings under 37 CFR 1.83(a) because the figures purportedly do not show every feature of the claimed invention. The Examiner's attention is directed to 37 CFR 1.81(a), which states that drawings are only required when "necessary for the understanding of the subject matter sought to be patented." In the present case, drawings are not necessary for a person of ordinary skill in the art to understand the claimed tissue

marker. Rather, Figs. 1-6 were provided to further demonstrate the results of the Examples, in which the claimed marker was shown to be visible under various imaging modalities without substantial distortion. As such, these drawings fall under 37 CFR 1.83(c), pursuant to which drawings may be submitted to further illustrate an invention even when not required under § 1.83(a).

Nonetheless, Applicants have submitted as part of this Amendment replacement Figures 1-11. Figures 1-5 are new, and show examples of markers according to embodiments of the present invention. Support for these drawings can be found at page 13. Figures 6-11 are the same as original Figures 1-6.

#### Amendment to the Specification

An amendment to the specification has been included to describe new figures 1-6. Support for this amendment can be found at page 13.

#### Rejections under 35 U.S.C. § 102

Claims 1-3, 5-32, 35, 39-67 and 70-83 stand rejected as being anticipated by U.S. patent 6,394,965 to Klein ("Klein"). The Examiner asserted that Klein discloses a method of tissue marking by implanting microparticles comprising carbon-coated zirconium oxide and imaging under x-ray, mammography and MRI. Applicants respectfully submit that this rejection should be withdrawn for the reasons set forth below.

Amended independent claims 82 and 89 each recite a marker consisting of a single zirconium oxide substrate or body, which has an elongate shape and a length between about 800 and about 3500 microns such that it is distinguishable from features of an anatomical site. The claimed marker provides multiple benefits not taught in the prior art. One benefit is that the claimed marker is imageable under multiple imaging modalities using a solid homogenous particulate or substrate material, as opposed to certain markers disclosed in the prior that require multiple contrast agents and/or particles to achieve multi-modalities capabilities. Another benefit is that, as demonstrated in the examples, the claimed marker is

detectable under magnetic imaging modalities without substantial distortion. Certain prior art multi-modality markers produce substantial image distortion.

The Klein patent clearly recites a method of marking a tissue site by injecting *a plurality of microparticles*, and not a single substrate or body as required by claims 82 and 89. Moreover, these claims also recite that the marker has an elongate shape and a length between about 800 and about 3500 microns so as to be distinguishable from features of the anatomical site under x-ray imaging. As noted in the specification, sizing and shaping the marker in this manner distinguishes the marker from anatomical features such as calcifications (page 13, lines 9-15) under x-ray imaging.

Although the Klein patent teaches a range of microparticle sizes, it does not teach, suggest or recognize a single substrate or body having the claimed shape and size that is distinguishable from features of an anatomical site under x-ray imaging as compared to a plurality of microparticles. As described in the enclosed Declaration of Dean Klein ("the Klein Declaration"), an experiment using an embodiment of the microparticles described in the Klein patent demonstrated that the microparticles were visible, but not distinguishable from features of the anatomical site under x-ray imaging. For example, the microparticles were not distinguishable from microcalcifications, which are often present at tissue sites to be marked.

A person of skill in the art would not have reasonably expected based on the teachings of the Klein patent that a tissue marker having the features recited in claims 82 and 89 would be distinguishable from anatomical features under x-ray, particularly when the microparticles described in the Klein patent were not. Accordingly a person of ordinary skill in the art would not have had any basis or reason for modifying the microparticles disclosed in the Klein patent to achieve the invention recited in claims 82 and 89.

Moreover, the Klein patent does not disclose, suggest or recognize an unexpected benefit of the present invention that the claimed marker is imageable under multiple imaging modalities including magnetic imaging modalities. The Klein patent teaches that zirconium oxide is radiopaque (i.e., not transparent to x-rays), but does not teach or suggest that a single zirconium oxide substrate or body is imageable under magnetic resonance imaging without

substantial distortion. Rather, the Klein patent only generally teaches that the use of different types of contrast agents will affect the imaging modality under which the microparticles are detectable. Based on this, person of ordinary skill in the art would not reasonably expect to achieve imaging under multiple modalities by modifying the microparticles disclosed in the Klein patent to provide a single zirconium oxide substrate or body. Applicants respectfully request withdrawal of this rejection.

With respect to method claims 90 and 91, the Klein patent does not teach a method of marking a tissue site using only a single zirconium oxide substrate or body, or imaging that tissue site under x-ray and magnetic imaging. The Klein patent, as noted above, teaches the injection of multiple microparticles at the tissue site, and fails to teach that a zirconium oxide is imageable under magnetic resonance imaging. Based on this, person of ordinary skill in the art would not reasonably expect to achieve imaging under multiple modalities by modifying the microparticles disclosed in the Klein patent to provide a single zirconium oxide substrate or body. Applicants respectfully request withdrawal of this rejection.

Although McCrory also cited by the Examiner teaches a multi-modality marker and method, it achieves this result by providing a capsule that can contain various liquid contrast agents depending on the desired imaging modalities. Accordingly, the combination of the Klein patent and McCrory at best teaches combining various materials to achieve multi-modality imaging. It does not teach or suggest that multi-modality imaging can be achieved by a single zirconium oxide substrate or body.

#### Rejections Under 35 U.S.C. §103

Claims 35, 39-41, 68 and 69 stand rejected as being obvious in view of the Klein patent. Claims 33, 34 and 36-38 stand rejected as being obvious in view of Klein and U.S. application 2001/0004395 to McCrory ("McCrory"). Each of these claims has either been cancelled or amended to depend from one of the independent claims discussed above. Accordingly, this rejection should be withdrawn for the same reasons set forth above.

Conclusion

All of the claims remaining in this application are in condition for allowance. A prompt notice to that effect is respectfully solicited. If there are any remaining questions, the Examiner is requested to contact the undersigned at the number listed below.

Respectfully submitted,

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